Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

1. - 57. (Canceled)

58. (New) An isolated nucleic acid comprising a polynucleotide encoding a fragment of the polypeptide of SEQ ID NO:2, or a variant thereof, wherein said polypeptide is capable of decreasing inhibition of axonal growth of a central nervous system neuron.

59. (New) The isolated nucleic acid of claim 58, comprising a polynucleotide encoding a polypeptide selected from the group consisting of:

(a) a polypeptide comprising amino acids 34-532 of SEQ ID NO:2;
(b) a polypeptide comprising amino acids 34-417 of SEQ ID NO:2;
(c) a polypeptide comprising amino acids 34-432 of SEQ ID NO:2;
(d) a polypeptide comprising amino acids 417-531 of SEQ ID NO:2;
(e) a polypeptide comprising amino acids 425-531 of SEQ ID NO:2;
(f) a polypeptide comprising amino acids 1-531 of SEQ ID NO:2;
(g) a polypeptide comprising amino acids 433-493 of SEQ ID NO:2;
(h) a polypeptide comprising an Sp35 LRR domain, an Sp35 basic region C-terminal to the LRR domain, and an Sp 35 immunoglobulin (Ig) domain C-terminal to the basic region, but lacks a transmembrane domain;
(i) a polypeptide comprising an Sp35 Ig domain, but lacking an Sp35 LRR domain, an Sp35 basic region, a transmembrane domain, and a cytoplasmic domain;
(j) a polypeptide comprising an Sp35 LRR domain, but lacking an Sp35 Ig domain, an Sp35 basic region, a transmembrane domain, and a cytoplasmic domain;
(k) a polypeptide comprising an Sp35 LRR domain, basic region, Ig domain, connecting sequence, and transmembrane domain; but lacking a functional cytoplasmic domain;
(l) a polypeptide as in (h), further lacking a cytoplasmic domain;
(m) a polypeptide comprising amino acids 417 to 424 of SEQ ID NO:2;

(n) a polypeptide comprising amino acids 494 to 551 of SEQ ID NO:2;
(o) a polypeptide comprising amino acids 1-576 of SEQ ID NO:2;
(p) a polypeptide comprising amino acids 454-458 of SEQ ID NO:2;
(q) a polypeptide comprising amino acids 453-458 of SEQ ID NO:2;
(r) a polypeptide comprising the amino acids of SEQ ID NO:11 (ITPKRR);
(s) a polypeptide comprising the amino acids of SEQ ID NO:12 (ACPHHK); and
(t) a polypeptide comprising the amino acids of SEQ ID NO:13 (VSPRKH);

wherein said polypeptide is capable of decreasing inhibition of axonal growth of a central nervous system neuron.

60. (New) The nucleic acid of claim 58, further comprising a polynucleotide encoding a heterologous polypeptide fused to said polypeptide.

61. (New) The nucleic acid of claim 60, wherein said heterologous polypeptide is selected from the group consisting of an Ig polypeptide, a serum albumin polypeptide, a targeting polypeptide, a reporter polypeptide, a human NgR1-binding polypeptide, one or more cysteine residues and a purification-facilitating polypeptide.

62. (New) The nucleic acid of claim 61, wherein said heterologous polypeptide is selected from the group consisting of immunoglobulin Fc, human serum albumin or fragment thereof, a histidine tag, an oligodendrocyte-myelin glycoprotein or fragment thereof, a myelin associated glycoprotein or fragment thereof, and a Nogo 66 glycoprotein or fragment thereof.

63. (New) The nucleic acid of claim 61, wherein said polypeptide is cyclized.

64. (New) A composition comprising a pharmaceutically acceptable carrier and the nucleic acid of claim 58.

65. (New) A vector comprising the nucleic acid of claim 58.

66. (New) The vector of claim 65, wherein said nucleic acid is operatively linked to an expression control sequence.

67. (New) The vector of claim 66, wherein said vector is a viral vector.

68. (New) The vector of claim 67, wherein said viral vector is selected from the group consisting of an adenoviral vector, a lentiviral vector, a baculoviral vector, an Epstein Barr viral vector, a papovaviral vector, a vaccinia viral vector, and a herpes simplex viral vector.

69. (New) A host cell comprising the vector of claim 66.

70. (New) The host cell of claim 69, which expresses said polypeptide.

71. (New) An isolated polypeptide encoded by the nucleic acid of claim 58.

72. (New) The polypeptide of claim 71, wherein said polypeptide is produced synthetically.

73. (New) The polypeptide of claim 71, wherein said polypeptide is cyclized.

74. (New) The polypeptide of claim 71, wherein said polypeptide is conjugated to a polymer.

75. (New) The polypeptide of claim 74, wherein said polymer is selected from the group consisting of a polyalkylene glycol, a sugar polymer, and a polypeptide.

76. (New) The polypeptide of claim 75, wherein said polyalkylene glycol is polyethylene glycol (PEG).

77. (New) The polypeptide of claim 74, wherein said polypeptide is conjugated to 1, 2, 3 or 4 polymers.

78. (New) The polypeptide of claim 77, wherein the total molecular weight of the polymers is from 20,000 Da to 40,000 Da.

79. (New) An antibody or antigen-binding fragment thereof, which specifically binds to the polypeptide of claim 71, wherein said antibody or antibody-binding fragment decreases inhibition of axonal growth of a central nervous system (CNS) neuron.

80. (New) A composition comprising a pharmaceutically acceptable carrier and an active ingredient selected from the group consisting of the polypeptide of claim 71, an antibody or antibody fragment thereof which specifically binds to said polypeptide of claim 71, and a combination of said polypeptide, antibody or antibody fragment thereof wherein said polypeptide, antibody or antibody fragment decreases inhibition of axonal growth of a central nervous system (CNS) neuron.

81. (New) The composition of claim 80, further comprising a supplementary active compound selected from the group consisting of an anti-NgR1 antibody or binding fragment thereof and a soluble NgR1 polypeptide.

82. (New) A method of inhibiting signal transduction by NgR1, comprising contacting an NgR1-expressing cell with a therapeutically effect amount of the composition of claim 80.

83. (New) A method of decreasing inhibition of axonal growth of a central nervous system (CNS) neuron, comprising contacting said neuron with a therapeutically effective amount of the composition of claim 80.

84. (New) A method of inhibiting growth cone collapse of a CNS neuron, comprising contacting the neuron with a therapeutically effective amount of the composition of claim 80.

85. (New) A method of promoting survival of a neuron at risk of dying, comprising contacting said neuron with a therapeutically effective amount of the composition of claim 80.

86. (New) A method of treating a CNS disease, disorder or injury in a mammal in need thereof comprising administering to said mammal a therapeutically effective amount of the composition of claim 80.

87. (New) The method of claim 86, wherein said CNS disease, disorder or injury is selected from the group consisting of multiple sclerosis, ALS, Huntington's disease, Alzheimer's disease, Parkinson's disease, diabetic neuropathy, stroke, traumatic brain injury, optic nerve injury and spinal cord injury.

88. (New) A method of promoting myelination at the site of a CNS disease, disorder or injury comprising administering to a mammal in need thereof a therapeutically effective amount of the composition of claim 80.

89. (New) A method for treating a CNS disease, disorder or injury in a mammal comprising introducing the host cell of claim 70 into a mammal in need thereof at or near the site of the CNS disease, disorder or injury.

90. (New) The method of claim 89, wherein said host cell is derived from the mammal to be treated.

91. (New) A method for treating a CNS disease, disorder or injury in a mammal comprising administering to a mammal in need thereof a vector comprising the nucleic acid of claim 58, wherein said vector expresses the polypeptide encoded by said nucleic acid in an amount sufficient to reduce inhibition of axonal extension at or near the site of said CNS disease, disorder or injury.

92. (New) The method of claim 91 wherein said vector is a viral vector.

93. (New) The method of claim 92, wherein the viral vector is selected from the group consisting of an adenoviral vector, a lentiviral vector, a baculoviral vector, an Epstein Barr viral vector, a papovaviral vector, a vaccinia viral vector, and a herpes simplex viral vector.

94. (New) The method of claim 92, wherein the viral vector is administered by a route selected from the group consisting of topical administration, intraocular administration, parenteral administration, intrathecal administration, subdural administration and subcutaneous administration.

95. (New) The method of claim 91, wherein the CNS disease, disorder or injury is selected from the group consisting of multiple sclerosis, ALS, Huntington's disease, Alzheimer's disease, Parkinson's disease, diabetic neuropathy, stroke, traumatic brain injury, optic nerve injury and spinal cord injury.

96. (New) An isolated interfering RNA molecule comprising a nucleic acid which specifically binds to the polynucleotide of claim 58, wherein said interfering RNA molecule decreases inhibition of axonal growth of a central nervous system neuron.

97. (New) The interfering RNA molecule of claim 96, which is encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:41 and SEQ ID NO:42.

98. (New) A composition comprising the interfering RNA molecule of claim 96 and a pharmaceutically acceptable carrier.

99. (New) A method for the treatment of a CNS disease, disorder or injury comprising administering to a mammal in need thereof the interfering RNA molecule of claim 96.

100. (New) A method for producing an Sp35 polypeptide comprising culturing the host cell of claim 70 and recovering said Sp35 polypeptide from the culture medium.